REMARKS

Claims 25-26 and 28 are pending in this application. Claims 1-24 have been cancelled as being drawn to the non-elected invention. Claims 25-26 and 28 are rejected. No claim is objected to. Applicants amend claims 25 and 28 herein. Support for amended claims 25 and 28 can be found at pages page 6, lines 4-15, as well as originally filed claim 8. Claim 29 is added herein. Support for newly added claim 29 can be found at page 16, lines 18-22. Thus, no new matter is added.

In view of the following amendment and response, Applicants believe the claims presented herein are allowable. Reconsideration is respectfully requested.

SEQUENCE COMPLIANCE

A Sequence Error Report was submitted with the Office Action, requiring that Applicants provide a species of origin within the sequence listing and correct typographical errors relating to sequence identifiers for SEQ ID Nos: 12 and 13, at line 400. Applicants have herein amended the sequence listing to include a species of origin and corrected the errors as indicated in the Sequence Error Report. Both a paper and electronic copy of the sequence listing is sent to Mailstop: SEQUENCE.

35 U.S.C. §112, FIRST PARAGRAPH

Claims 25, 26 and 28 stand rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. The Examiner notes that Applicants have amended claims 25 and 28 to include the phrase "naturally occurring human." The Examiner also alleges that "the source of the enzyme cannot be concluded as that from human." The Examiner suggests that Applicants can overcome this rejection by canceling the phrase introduced into claim 25 and 28.

While the Applicant's believe that the recitation of "human" in the rejected claims is supported by the specification, for the avoidance of doubt, and to address the Examiner's comments, claims 25 and 28 have been amended herein to recite "human" in a manner that is unambiguously supported by the specification. These amendments in no way change the scope of the claims.

To illustrate why the Applicants believe that the word "human" was supported in the claims prior to amendment, the following discussion is provided. It is clear that the specification provides methods for isolating the coding sequences of the enzymes of the invention using a human genomic library. For example, see page 6, lines 22-28 of the specification. Furthermore, Example 6 demonstrates that expressed sequence tags (ESTs) from a human cDNA library have extensive alignments with the Sequences 1 and 3, isolated from plasma. See, for example, page 13 of the specification. SEQ ID NOs: 1 to 4 are described as isolated by plasma purification. See Example 4 page 12 of the specification. Furthermore, the complete sequence from cDNA of SEQ ID NO.:9 is described at page 15, lines 15-22 of the specification as well as in Figure 9. The skilled artisan would understand that a human cDNA library would be used to determine coding sequence isolated from a human sample. Thus, Applicants respectfully submit that they have provided adequate written description of the species from which the plasma of Example 4 and purified polypeptides were obtained. In addition, Applicants respectfully submit that they have provided adequate written description that the cDNA of SEQ ID NO.:9 is from human.

Claims 25, 26, and 28 stand rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the

application was filed, had possession of the claimed invention. Specifically, The Examiner alleges that "the recited structural feature of the genus (i.e., polypeptides comprising fragments such as SEQ ID NO:1, 2, or 10) does not constitute a substantial portion of the genus, the remainder of the structures of any polypeptides having the above activity is completely undefined and the specification does not define the reaming structural features necessary for members of the genus selected." Applicants respectfully submit that, as amended previously, claim 26 is directed to polypeptides that comprise SEQ ID NOs: 1, 2, and 4 rather than SEQ ID NOs: 1, 2, and 10 as the Examiner indicates. For the remainder of this response, Applicants assume that the Examiner intended to state that claim 26 is directed to SEQ ID NOs: 1, 2, and 4.

As a basis for rejecting Claims 25, 26, and 28, the Examiner refers to the revised guidelines concerning compliance with the written description requirement of 35 U.S.C. § 112, first paragraph and published in the Official Gazette. Specifically, the Examiner notes that, as discussed in the "written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." The Examiner goes on to allege that "one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed." The Examiner also alleges that the genus of the claims are "structurally diverse

(even when claimed from a single source, i.e., human) as it encompasses variants, mutants and recombinants."

Applicants have herein amended claims 25 and 28 to recite that the claimed lipoprotein associated phospholipase A2 is "encoded by a polynucleotide having at least 90% sequence identity with ... human SEQ ID NO:9." Support for these amendments can be found, for example, at page 6, lines 4-15, as well as in originally filed claim 8. Applicants respectfully submit that, as amended, claims 25 and 28 recite substantial structural, chemical and functional characteristics of the claimed lipoprotein associated phospholipase A2 and thus meet the written description requirement. Furthermore, because claim 26 depends from amended claim 25, it also meets the written description requirements.

Applicants further submit that the cited guidelines merely provide suggestions for Examiners in determining adequate written description. They certainly do not mandate that certain requirements be met in each application, as they are not, *per se*, legal requirements. That said, it is important to note that not even the text of the cited guidelines requires that a species of a genus be reduced to practice. The text merely suggests that a claimed genus "may be" satisfied by an actual reduction to practice of several representative species, which, in any case, the specification indeed furnishes. See, for example, Example 5, provided on pages 12-13 of the specification. The guidelines also provide that "there may be situations where one species adequately supports a genus....A 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." Applicants respectfully submit that the claims recite a genus wherein each member of the genus

possesses physical and chemical characteristics shared by other members, *viz.* a specific sequence, purity level and enzymatic activity. The skilled artisan would recognize that Applicants were in possession based on these common attributes of the disclosed species. For example, Applicants provide each lipoprotein associated phospholipase A2 enzyme encoded by a polynucleotide having a given sequence identity with SEQ ID NO:9.

Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejection under 35 U.S.C. §112, first paragraph, and the rejection should be withdrawn.

REJECTIONS UNDER 35 U.S.C. §102(b)

Claims 25-28 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Steinbrecher, *et al.* (*Journal of Lipid Research*, Vol. 30(3): 305-315 (1989))(hereinafter referred to as "Steinbrecher") or Stremler, *et al.* (*Journal of Biological Chemistry*, Vol. 264(10): 5331-5334 (1989))(hereinafter referred to as "Stremler"). Applicants traverse this rejection.

Specifically, the Examiner alleges that Stremler and Steinbrecher disclose an "identical enzyme called PAF-acetylhyrdrolase with characteristics identical to that claimed here (i.e, identical source, activity and molecular weight)." The Examiner goes on to concede that the cited references do not provide amino acid or nucleotide sequences encoding said enzyme. In fact, neither reference teaches any sequence. However, based on the activity and the source of the enzyme the Examiner "takes the position that the characteristic such as amino acid sequence is an inherent characteristic of any protein or enzyme and therefore the enzyme in the reference and the instant enzyme claimed are one and the same." In so noting, the Examiner has bootstrapped an indentity between the activity in the cited art and the lipoprotein associated phospholipase A2 of the claimed

invention. There is nothing in the art that requires this identity. That is the sole basis on which the Examiner can then argue, in essence, that the same proteins possess the same sequence. This a surprising position for the Examiner to take in view of his earlier contention that in claims 25 and 28, "the source of the enzyme cannot be concluded as that from human."

The Examiner further alleges that "the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F. 2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald, et al.*, 205 USPQ 594." It is the Applicants' position that this burden shifting is improper based on the instant facts. Applicants reason for this view is that the right of the Patent Office to shift the burden of proof to the Applicant is based on its inability to "manufacture the products or compare products" of the cited art with the claimed invention. *In re Best*, 562 F. 2d 1252 at 1255. If this right is invoked the Office may require that Applicants "prove that the prior art products do not ***necessarily*** or inherently possess the characteristics of his claimed product." *Id.* This requirement differs from showing a "novel or unobvious difference between the claimed product and the product of the prior art." as the Examiner suggests in the Office Action. Before shifting the burden of proof to the Applicant, the Examiner must reasonably assert inherency.

Inherent anticipation may only be asserted under 102(b) if all of the claimed elements are "found within the four corners of that single publication, either expressly or inherently, as it is understood by the hypothetical person of ordinary skill in the art." See *ATD Corp. v. Lydall Inc.*, 159 F.3d 534, 545 (Fed. Cir. 1998*); Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576-77 (Fed. Cir. 1991)" *Astra Aktiebolag v. Andrx Pharmaceuticals, Inc.*, 222 F. Supp. 2d 423 (SDNY 2002). Inherent anticipation

arises when "the prior art ***necessarily*** functions in accordance with, or includes, the claimed limitations," *Atlas Powder Co v. IRECO Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999).* Emphasis added. Applicants respectfully submit that certainty is required in establishing inherent anticipation. It is well-settled law that inherent anticipation "may not be established by probabilities or possibility." See *Hansgrig v. Kimmer*, 102 F.2d 212 (CCPA 1939), *In re Zierden*, 411 F.2d. 1325, (CCPA 1969), and *In re Oelrich, et al.* 66 F.2d 578 (CCPA 1981).

Therefore, before shifting the burden of proof to the Applicants, the Examiner must reasonably assert inherency, and this assertion must be based on certainty and not on probability. That was not done by the Examiner as evidenced by [his/her] statement that there is an "equal possibility that the proteins of the reference have the same amino acid sequence as claimed or at least comprise the sequence of fragments in claim 26." This assumption is not based on certainty but merely on probability. In turn, the logical corrollary to the Examiner's view is that there is an equal possibility that the proteins of the cited art do not comprise the fragments of claim 26. Thus, the Examiner has not carried his burden of making out a *prima facie* case of inherence prior to shifting the burden to the Applicants.

Applicants also submit that facts of the instant case differ from the facts presented in *In re Best, supra* and relied upon by the Examiner. In *In re Best*, all process limitations of the claim at issue were expressly disclosed in the cited art except "for the functionally expressed rate of cooling." However, the court noted that "because any sample of Hansford's calcined zeolitic catalyst would necessarily be cooled to facilitate subsequent handling, the conclusion of the examiner that such cooling is encompassed by the terms of the appealed claims was reasonable." In the instant application the sequence of the

proteins in the cited art, which are not disclosed, do not necessarily comprise the sequences of the claimed polypeptides. As noted above, the Examiner concedes that it is possible that a polymorphism may exist in a naturally occurring polypeptide. Thus, the sequences of the cited art do not necessarily comprise the sequences of the instant application.

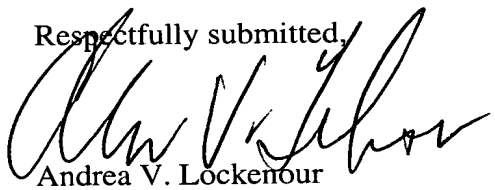
Finally, inherent anticipation requires that the missing descriptive material is recognized by a person of ordinary skill in the art as "necessarily present in the thing." *Continental Can v. Monsanto Company*, 948 F.2d 1264, (Fed. Cir. 1991). Thus, the resulting method must be understood by the skilled artisan to be the certain result or necessarily result in the disclosure of the prior art. As was discussed above and noted by the Examiner, enzymes with similar activities and derived from the same source can have varied amino acid sequences. As was previously presented, Campbell, *et al.* (WO 02/36817, SmithKline Beecham PLC) describe polymorphisms or naturally occurring variations in DNA sequences within an organism which may or may not manifest in an observed phenotype. Specifically, Campbell, *et al.*, describe polymorphisms that naturally occur within LPA-PLA2 at position 379. Furthermore, Campbell, *et al.* also cite Cousens, *et al.* (WO 95/09921, ICOS Corporation) which discloses another known polymorphism of LPA-PLA2 at position 279. Because polymorphisms are known to occur naturally in Lp-PLA2 from human, Applicants respectfully submit that it would not be reasonable for the skilled artisan to assume that the sequences of polypeptides disclosed in Steinbrecher, *et al.* or Stremler, *et al.* would be identical to each other or to the sequences claimed in the instant application. Therefore, these two references cannot inherently anticipate the claims of the present case as they do not necessarily include each and every element of the claims.

Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejection under 35 U.S.C. §102(b), and the rejection should be withdrawn.

Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited.

If it would expedite the prosecution of this application, the Examiner is invited to confer with Applicants' undersigned attorney.

Respectfully submitted,



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